

Please add the following new claims:

ad --58. A vector construct comprising a transcriptional regulatory sequence operably linked to a translational start codon, a secretion signal sequence, an epitope tag, a sequence-specific protease site, and an unpaired splice donor site.

59. The vector construct of claim 58, wherein said construct further comprises one or more amplifiable markers.

60. The vector construct of claim 58, wherein said transcriptional regulatory sequence is a promoter.

61. The vector construct of claim 60, wherein said promoter is a viral promoter.

62. The vector construct of claim 61, wherein said viral promoter is a cytomegalovirus immediate early gene promoter.

63. The vector construct of claim 61, wherein said promoter is a non-viral promoter.

64. The vector construct of claim 61, wherein said promoter is an inducible promoter.

65. A cell containing the vector construct of claim 58.

66. A cell containing the vector construct of claim 59.

67. The cell of claim 65, wherein said vector construct has integrated into the cellular genome.

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68. The cell of claim 66, wherein said vector construct has integrated into the cellular genome.

69. The cell of claim 67 or 68, wherein an endogenous gene is over-expressed in said cell by upregulation of the gene by said transcriptional regulatory sequence on said vector construct.

70. The cell of claim 65, wherein said cell is an isolated cell.

71. The cell of claim 66, wherein said cell is an isolated cell.

72. A method for making a host cell, comprising introducing the construct of claim 58 into a cell.

73. A method for producing an expression product of an endogenous cellular gene or portion thereof comprising:

- (a) introducing the construct of claim 58 into a genome-containing cell;
- (b) integrating said construct into the genome of said cell by non-homologous recombination; and
- (c) over-expressing said endogenous gene in said cell.

74. The method of claim 73, wherein said over-expression is accomplished *in vitro*.

75. The method of claim 73, wherein said over-expression is accomplished *in vivo*.

76. The method of claim 73, further comprising isolating said expression product from said cell.

77. A cell library comprising a collection of cells transformed with the construct of claim 58, wherein said construct is integrated into the genomes of said cells by non-homologous recombination.

78. A method of obtaining a gene product from a library of cells comprising screening the library of claim 77 for expression of said gene product, selecting from said library a cell that over-expresses said gene product, and obtaining said gene product from said selected cell.

79. A method for producing an expression product of an endogenous cellular gene comprising:

- (a) introducing a vector comprising a transcriptional regulatory sequence operably linked to a secretion signal sequence and an unpaired splice donor sequence into a cell;
- (b) integrating said vector into the genome of said cell by non-homologous recombination;
- (c) over-expressing an endogenous gene or a portion thereof in said cell by upregulation of said gene by said transcriptional regulatory sequence;
- (d) screening said cell for over-expression of said endogenous gene or portion thereof; and
- (e) culturing said cell under conditions favoring the production of the expression product of said endogenous gene or portion thereof by said cell.

80. The method of claim 79, further comprising isolating said expression product.

81. A method for over-expressing an endogenous gene in a cell *in vivo*, comprising:

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- (a) introducing a vector comprising a transcriptional regulatory sequence into a cell;
  - (b) integrating said vector into the genome of said cell by non-homologous recombination;
  - (c) over-expressing an endogenous gene or a portion thereof in said cell by upregulation of said gene by said transcriptional regulatory sequence;
  - (d) screening said cell for over-expression of said endogenous gene; and
  - (e) introducing said isolated and cloned cell into an animal under conditions favoring the overexpression of said endogenous gene by said cell *in vivo*.

82. A method for producing an expression product of an endogenous cellular gene *in vivo*, comprising

- (a) introducing a vector comprising a transcriptional regulatory sequence operably linked to an unpaired splice donor sequence into a cell;
- (b) integrating said vector into the genome of said cell by non-homologous recombination;
- (c) over-expressing an endogenous gene or a portion thereof in said cell by upregulation of said gene by said transcriptional regulatory sequence;
- (d) screening said cell for over-expression of said endogenous gene; and
- (e) introducing said isolated and cloned cell into an animal under conditions favoring the overexpression of said endogenous gene by said cell *in vivo*.

Sub B<sup>1</sup> 83. The method of any one of claims 79, 81 or 82, wherein said transcriptional-regulatory sequence is a promoter.

84. The method of claim 83, wherein said promoter is a viral promoter.

85. The method of claim 84, wherein said viral promoter is the cytomegalovirus

immediate early promoter.

86. The method of claim 83, wherein said promoter is a non- viral promoter.

87. The method of claim 83, wherein said promoter is inducible.

98 Sub B<sup>2</sup> 88. ~~The method of any one of claims 79, 81, or 82, further comprising introducing double strand breaks into the genomic DNA of said cell prior to or simultaneously with integration of said vector.~~

89. ~~The method of claim 72, further comprising introducing double strand breaks into the genomic DNA of said cell prior to or simultaneously with integration of said vector.~~

90. ~~The method of claim 73, further comprising introducing double strand breaks into the genomic DNA of said cell prior to or simultaneously with integration of said vector.~~

91. ~~A gene expression product produced by the method of any one of claims 79, 81, or 82.~~

92. ~~The method of any one of claims 79, 81, or 82, wherein said vector construct is linear.~~

93. A method for producing an expression product of an endogenous gene in a cell comprising:

- (a) introducing a vector comprising a transcriptional regulatory sequence into at least one isolated genome-containing cell;
- (b) integrating said vector into the genome of said cell by non-homologous recombination;

- (c) over-expressing an endogenous gene or a portion thereof in said cell by upregulation of said gene by said transcriptional regulatory sequence;
- (d) screening said cell for over-expression of said endogenous gene; and
- (e) culturing said cell in reduced serum medium.

94. A method of protein discovery comprising:

- (a) introducing a vector comprising a transcriptional regulatory sequence into at least one isolated genome-containing cell;
- (b) integrating said vector into the genome of said cell by non-homologous recombination;
- (c) culturing said cell in reduced serum medium under conditions that allow over-expression of an endogenous gene or a portion thereof in said cell by upregulation of said gene by said transcriptional regulatory sequence, thereby producing cell-conditioned media; and
- (d) screening said cell-conditioned media for the presence of the expression product of said gene or portion thereof.

95. The method of claim 94, further comprising concentrating said cell-conditioned media prior to screening in (d).

96. The method of any one of claims 93-95, wherein said method comprises a high-throughput assay.

97. A method for producing an expression product of an endogenous cellular gene comprising:

- (a) introducing a vector comprising a transcriptional regulatory sequence into a cell;
- (b) integrating said vector into the genome of said cell by non-homologous

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recombination;

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- (c) over-expressing an endogenous gene or a portion thereof in said cell by upregulation of said gene by said transcriptional regulatory sequence;
  - (d) screening said cell for over-expression of said endogenous gene; and
  - (e) culturing said cell under conditions favoring the production of the expression product of said endogenous gene by said cell; and
  - (f) isolating said expression product from a cell mass equivalent to at least 10 liters of cells at  $10^4$  cells/ml.

98. The method of any of claims 93-95 and 97, wherein said vector further comprises one or more amplifiable markers.

99. The method of any of claims 93-95 and 97, wherein said vector further comprises an unpaired splice donor site.

Sub 84 100. The method of any one of claims 76, 79, 81, 82, 93-95, and 97, wherein said endogenous gene encodes a transmembrane protein.

101. The method of either of claims 81 or 82, further comprising isolating and cloning said cell prior to introducing said cell into an animal.

102. The method of either of claims 81 or 82, wherein said animal is a mammal.

103. The method of claim 102, wherein said mammal is a human.

104. A method for activating expression from an endogenous gene comprising:

- (a) introducing into a chromosome-containing host cell a vector suitable for activating an endogenous gene;